REMARKS/ARGUMENTS

By the present amendment, claim 1 has been amended to include the subject matter of claims 21 and 22 which have been deleted. In addition, claims 8-10 have been amended to insert the term "agent" after "active" to be consistent with claim 1. Claims 23, 24, 29, 30 and 32 have been amended to correct improper dependencies.

The amendments to the claims have been made without prejudice and without acquiescing to any of the Examiner's objections. Applicant reserves the right to pursue any of the deleted subject matter in a further divisional, continuation or continuation-in-part application. No new matter has been entered by the present amendment and its entry is respectfully requested.

The office action dated January 28, 2010 has been carefully considered. It is believed that the amended claims and the following comments represent a complete response to the Examiner's rejections and place the present application in condition for allowance. Reconsideration is respectfully requested.

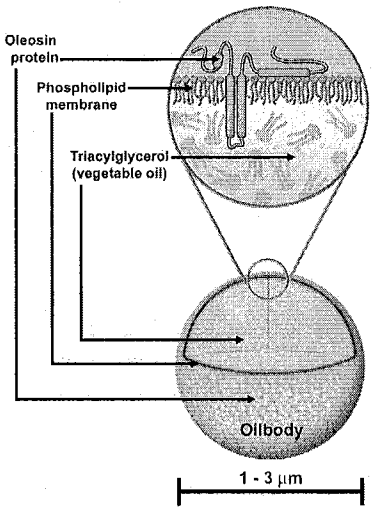
Election/Restrictions

The Examiner has objected to claims 29, 30 and 32 as having improper dependencies. In response, claim 29 has been amended to depend on claim 28, claim 30 has been amended to depend on claim 29 and claim 32 has been amended to depend on claim 31.

35 USC §102

To assist in addressing the outstanding office action, it may be useful to briefly summarize the invention. The present invention relates a new system for oil body partitioning of actives agents. As described in US 2007/0196914 Al (hereinafter "the present application"), on page 1, paragraph [0002], oil bodies are discrete subcellular oil

or wax storage organelles which are found in animal, plant, fungal, yeast, bacterial and algae cells. Below is a schematic of an oil body.



Oil bodies are made up of an internal triacylglycerol core and a phospholipid membrane. The current invention provides for one or more hydrophobic and/or amphipathic actives of interest to partition into the internal triacylglyerol (oil) core, onto the lipid membrane, into the lipid membrane or attached to the external surface of the lipid membrane of the oil body. The system involves the use of two-solvents and solubilization of an active resulting in the blending of the active and the oil body emulsion. The system is more complex than simply mixing the oil body emulsion with the active agents and results in increased active partitioning onto or into the oil bodies. This is especially useful for partitioning solid and semi-solid, hydrophobic and amphipathic molecules that are particularly difficult to solubilize, often requiring the use of organic solvents

As described in the present application on page 2, paragraphs [0010] to [0013]) and in claim 1, the present invention provides a method for partitioning of active agents into oil bodies comprising the following three steps:

(1) dissolving the active agent in a first solvent;

(2) mixing the dissolved active agent with a second solvent to obtain a mixture of the first and second solvent comprising the active agent; and

(3) contacting said mixture of the first and second solvent with oil bodies to partition said active agent into said oil bodies to partition said active agent into said oil bodies.

The Examiner has objected to claims 1-22, 25 and 31-34 under 35 USC §102b as being anticipated by Deckers et al. (US 6,372,234 B1). In particular, the Examiner alleges that Deckers et al discloses a method of partitioning an active into oil bodies comprising dissolving an active agent in oil to form an oil phase, mixing the aqueous phase with the oil phase to form an emulsion and mixing the emulsion with oil bodies (see Example 7). We respectfully disagree with the Examiner for the reasons that follow.

Deckers et al. describes a method for preparing emulsion formulations comprising oil bodies. As described in Example 7, an oil-in-water emulsion is created using standard formulation techniques wherein a water phase and oil phase were mixed vigorously using agitation at high temperatures with the addition of oil bodies once the temperature has decreased to approximately 40°C. The current application describes a new method for improved partitioning of an active agent into the oil body structure. The system involves the use of two solvents and solubilization of an active agent resulting in the blending of the active agent and the oil body emulsion. The system is more complex then mixing the oil body emulsions with the active ingredients (as described in Deckers et al.) and results in increased active partitioning onto or into the oil bodies. As described on page 5, paragraphs [0036] to [0038], the present application describes a method for partitioning an active agent into oil bodies by dissolving the active agent in a first solvent, mixing the dissolved active agent with a second solvent and then incubating oil bodies with the solvent/active mixture to facilitate partitioning of the active into the oil bodies. In order to more clearly differentiate the current claims over Deckers et al., claim 1 has been amended to indicate that the first solvent is an organic solvent selected from alcohols, aliphatic hydrocarbons, aromatic hydrocarbons, chlorinated hydrocarbons, glycols, glycol ethers and their acetates, esters, ethers and ketones. Deckers uses water or oil to dissolve the active agents, neither of which is an organic solvent as recited in claim 1. In order to anticipate, the prior art must contain **all** of the

limitations of the claims. As Deckers et al. does not teach the use of the recited organic solvents, it can not anticipate the claims.

The Examiner further states that Deckers et al. meets all of the limitations of claims 11-19 as Deckers et al. discloses clindamycin, retinoic acid, benzoyl peroxide, tetracaine and lidocaine as active agents and although Deckers is silent regarding the active agents have a log P value of 3.5 and a HLB value from about 1 to 14, from 4 to 10 and from 6 to 8, the active agents are the same as the active agents recited in the instant claims. We respectfully submit, that while Deckers has disclosed the above referenced active agents, claims 11-19 depend directly or indirectly from claim 1 which is not disclosed in Deckers et al. As described above, claim 1 has been amended to indicate that the first solvent is a specific organic solvent which is not disclosed in Deckers et al. Accordingly, Deckers et al. can not anticipate dependent claims 11-19.

In addition, the Examiner states that Deckers et al. meets all of the limitations of claims 21, 22 and 25 as Deckers et al. discloses that the first solvent is oil and the second solvent is water (Example 7). We do not understand this objection with respect to previous claim 21 as it specified that the first solvent is an organic solvent which has now been incorporated into claim 1. As noted above, Deckers does not use organic solvents. Claim 22 has been cancelled although some of the listed solvents have been incorporated in claim 1. Claim 25 depends from claim 1 and therefore has the novel features of claim 1. Therefore, Deckers et al., can not be said to anticipate claims 21, 22 or 25.

The Examiner has also stated that Deckers et al. meets all of the limitations of claims 31 to 34 in that Deckers et al., discloses that the oil bodies in the composition are obtained from safflower (Example 7). We respectfully submit, while oil bodies used in the current invention may be obtained by safflower, Deckers does not disclose the novel method of claim 1. As claims 31-34 depend directly or indirectly from claim 1, Deckers et al., can not be said to anticipate claims 31 to 34.

The Examiner has also stated that Deckers et al. meets all of the limitations of claims 2 to 4 and 20 in that while Deckers et al. is silent about the active agent not being partitioned into oil bodies when contact in the absence of a solvent or when the active agent is dissolved in the first solvent alone, the active being insoluble in water, the active being insoluble in the second solvent and the first solvent being non-compatible with oil bodies or undesirable in the final product, the first solvent, the second solvent, the active agents, the oil bodies and the method of producing the composition comprising a first solvent, a second solvent, active agents and oil bodies disclosed by Deckers et al. are the same as those recited in the instant claims and thus the active agent disclosed by Deckers et al. would necessarily possess the properties recited in the instant application. Again, claim 1 has been amended to specify that the first solvent is an organic solvent selected from alcohols, aliphatic hydrocarbons, aromatic hydrocarbons, chlorinated hydrocarbons, glycols, glycol ethers and their acetates, esters, ethers and ketones which is not disclosed in Deckers et al. As claims 2-4 and 20 depend directly or directly from claim 1, Deckers et al. can not said to anticipate claims 2 – 4 and 20.

The Examiner has also stated that Deckers et al. meets all of the limitations of claims 5-10 in that while silent about 0.1% of an active agent being partitioned into oil bodies and the efficiency of partitioning of an active agent being 40%. The first solvent, the second solvent, the active agents, the oil bodies and the methods of producing the composition comprising a first solvent, a second solvent, active agents and oil bodies are disclosed by Deckers et al. are the same as those recited in the instant claims and thus the composition disclosed by Deckers et al. would necessarily possess the properties recited in the instant claims: having 0.1% of an active agent being partitioned into oil bodies and 40% partitioning efficiency of an active agent. As previously stated, Deckers does not describe using an organic solvent as specified in claim 1. As claims 5-10 depend directly or indirectly from claim 1, Deckers et al. can not said to anticipate claims 5–10.

In view of the foregoing, we respectfully request that the objection to the claims under 35 USC §102b, be withdrawn.

35 USC §103

The Examiner has objected to claims 1, 23, 24, 26-29 under 35 USC §103(a) as being unpatentable over Deckers et al. (US 6,372,234 B1) in view of Gregoriadis (("Liposome Technology, Volume II, Incorporation of Drugs, Proteins and Genetic Material", 1983, p29) and Desai et al. (US 5,916,596) in that it would have been prima facie obvious at the time of the invention to a person of ordinary skill in the art to combine the teachings of Deckers et al., Gregoriadis and Desia et al. to choose chloroform as the first solvent and monobasic sodium phosphate as the second solvent.

We respectfully submit that, as described above, Deckers et al. describes a method for preparing emulsion formulations comprising oil bodies. The method involves the creation of an oil-in-water emulsion using standard formulation techniques wherein a water phase and oil phase were mixed vigorously using agitation at high temperatures with the addition of oil bodies once the temperature has decreased to approximately 40°C. No organic solvents are used. The current application describes a new method for improved partitioning of an active into an oil body. The system involves the use of two solvents and solubilization of an active resulting in the blending of the active and the oil body emulsion. The system is more complex then mixing the oil body emulsions with the active ingredients (as described in Deckers et al.) and results in increased active partitioning onto or into the oil bodies. Amended claim 1 relates to a method for partitioning an active agent into oil bodies by dissolving the active agent in a first solvent that is an organic solvent, mixing the dissolved active agent with a second solvent and then incubating oil bodies with the solvent/active mixture to facilitate partitioning of the active into the oil bodies. The inventors have demonstrated that the novel method leads to an improvement in the partitioning of active agents into oil bodies. In particular, the method is extremely useful in partitioning active agents that are normally difficult to solubilize. While Deckers et al. teach that oil bodies are useful in making emulsions,

Deckers et al. in no way teaches or suggests a novel method for partitioning active agents into oil bodies as recited in the present claims. Further, Deckers et al. provides no teaching or suggestion to one of skill in the art to use organic solvents to improve the partitioning of active agents into the oil bodies. In fact, Deckers et al. is a patent to the same Applicant as the present application and shares a common inventor. Had the inventors of Deckers et al. understood or predicted that using an organic solvent would have improved the preparation of emulsions containing active agents, it would have been mentioned in Deckers et al. However, at that time, the inventors had not realized that the partitioning could be improved which is clearly evidenced by the teachings of Deckers et al. Further, even if they had decided to try and improve partitioning of the active agent they would not have immediately thought of using an organic solvent as such solvents are generally not desirable in emulsions for topical application. Accordingly, the solution taught by the present application would have been counter-intuitive to one of skill in the art. The deficiencies in Deckers are clearly not remedied by Gregoriadis or Desai, alone or in combination.

The Examiner has indicated that while Deckers et al. do not specify chloroform as the first solvent and monobasic sodium phosphate as the second solvent and removing the first solvent by evaporation after it has been mixed with the second solvent that this deficiency is cured by Gregoriadis and Desai. We respectfully disagree with the Examiner for the reasons that follow.

First, the rejection is improper as it assumes that the difference between Deckers et al. and the present claims is the use of chloroform and monobasic sodium phosphate. These are limitations present in dependent claims 24 and 26 but are not present in claim 1 which is also under objection. As a result, the Examiner's analysis is based on preferred features and not the invention as a whole. As noted above, the difference between Deckers et al. and the present invention is that Deckers et al. does not teach a method to partition an active agent into oil bodies using the two solvent system recited in claim 1. Most importantly, Deckers et al. does not teach or suggest the use of an organic solvent as the first solvent.

Second, there is nothing in Gregoriadis and Desai when combined with Deckers et al. that would lead one of skill in the art to the present invention. The present application involves the use of naturally occurring structures called oil bodies. As described on page 1, paragraph [0002] of the present application, oil bodies are comprised of a mixture of triacyglycerides, phospholipids and a number of associated proteins, collectively termed oil body proteins. From a structural point of view, oil bodies are a triacylglyceride matrix encapsulated by a monolayer of phospholipids in which oil body proteins are embedded and form an outer shell. It should be noted that in this respect the proteins form a physical barrier separating the exterior of the oil body from the triacylglyceride matrix. It should also be noted that oil bodies are not a simple "lipid mixture" made my mixing different lipids together but are complex, naturally occurring, discrete subcellular structures that store the oil fraction of plant cells. The current application involves the use of a novel method for generating formulations comprising oil bodies and an active molecule partitioned into said oil bodies. In contrast, Gregoriadis uses purified chemical compounds to prepare a liposome comprising an active. In particular, the active is encapsulated in a REV (Reverse Phase Evaporation) liposome by forming the liposome around the active, for example Ara-A. As described on page 29, as Ara-A is hard to dissolve, DMSO is used to dissolve the Ara-A and an aqueous buffer of 10% PBS is added to the dissolved Ara-A. Separately, the phospholipids are dissolved in an organic solvent, isopropyl ether. The two solutions are mixed together using sonification to create a water-in-oil emulsion. The liposomes are formed around the Ara-A upon the removal of the organic solvent by rotary evaporation. Thus Gregoriadis does not disclose or even suggest that an active agent can partition into an oil body, let alone disclose the specific method of partitioning the active into the oil body claimed in the present application.

The deficiencies of Deckers et al, and Gregoriadis are in no way remedied by Desai which relates to a method for the formation of submicron particles (nanoparticles) of pharmacologically active agents by a solvent evaporation technique from an oil-in water emulsion. The method of Desai discloses a pharmacologically active agent dissolved in

a suitable solvent which is added to an oil phase (see column 9, lines 1 – 17). A protein is added to the aqueous phase to act as a stabilizing agent for the formation of stable nanodroplets (see column 9, lines 19 – 21), an emulsion is formed between the oil phase and the aqueous phase by homogenization under high pressure and high shear forces (column 9, line 27-28) and finally the solvent is evaporated under reduced pressure to yield a colloidal system composed of protein coated nanoparticles of pharmacologically active agent and protein (column 9, line 40 – 42). Thus Desai does not disclose or even suggest that an active agent can partition into an oil body, let alone disclose the specific method of partitioning the active into the oil body recited by Applicant.

In view of the foregoing, we respectfully request that the objection to the claims 1, 23, 24, 26-29 under 35 USC §103(a), be withdrawn.

The Examiner has objected to claim 30 under 35 USC §103(a) as being unpatentable by Deckers et al. (US 6,372,234 B1) in view of Gregoriadis (("Liposome Technology, Volume II, Incorporation of Drugs, Proteins and Genetic Material", 1983, p29) and Kaufman et al. (US 5,616,330) in that it would have been prima facie obvious at the time of the invention to a person of ordinary skill in the art to combine the teachings of Deckers et al., Gregoriadis and Kaufman et al. to remove the first solvent by exposing to a stream of nitrogen.

As described above, Deckers et al. in no way renders the present claims obvious. In addition, as Deckers et al. does not use an organic solvent selected from alcohols, aliphatic hydrocarbons, aromatic hydrocarbons, chlorinated hydrocarbons, glycols, glycol ethers and their acetates, esters, ethers and ketones. Deckers et al. in no way describes a method wherein the organic solvent is evaporated by exposing to a stream of nitrogen. Again, the Examiner is basing the objection on preferred features and not the invention as a whole as recited in the main claim.

In contrast, as discussed above in Gregoriadis, purified chemical compounds are used to prepare a liposome comprising an active agent. Thus Gregoriadis does not disclose or even suggest that an active can partition into an oil body, let alone disclose the specific method of partitioning the active into the oil body as described in claim 1 or the fact that the organic solvent can be evaporated by exposing to a stream of nitrogen recited by Applicant.

The deficiencies of Deckers et al, and Gregoriadis are in no way remedied by Kaufman which relates to a method for the incorporation of taxine into an oil and making a stable oil-in-water emulsion. The method of Kaufman discloses dissolving taxol in an alcohol solution, adding the solution to an equivalent volume of oil and mixing until clear. The alcohol is then removed by rotary evaporation or evaporation under a stream of nitrogen (see column 4, lines 26 – 33). Subsequently a phosopholipid containing aqueous phase is stirred a high speed with the oil solution containing taxol to create an emulsion (see column 4, lines 34 – 41). Thus Kaufman does not disclose or even suggest that an active agent can partition into an oil body, let alone disclose the specific method of partitioning the active into the oil body recited by the present claims.

In view of the foregoing, we respectfully request that the objection to the claim 30 under 35 USC §103(a), be withdrawn.

The Commissioner is hereby authorized to charge any fee (including any claim fee) which may be required to our Deposit Account No. 02-2095.

In view of the foregoing comments and amendments, we respectfully submit that the application is in order for allowance and early indication of that effect is respectfully requested. Should the Examiner deem it beneficial to discuss the application in greater

detail, he/she is kindly requested to contact the undersigned by telephone at (416) 957-1682 at his/her convenience.

Respectfully submitted,

Bereskin & Parr LLP/
S.E.N.C.R.L., s.r.l.

By _____
Micheline Gravelle
Reg. No. 40,261

40th Floor
40 King Street West
Toronto, Ontario
Canada M5H 3Y2

Tel: 416-957-1682
Fax: 416-361-1398